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# BIOCHEMISTRY

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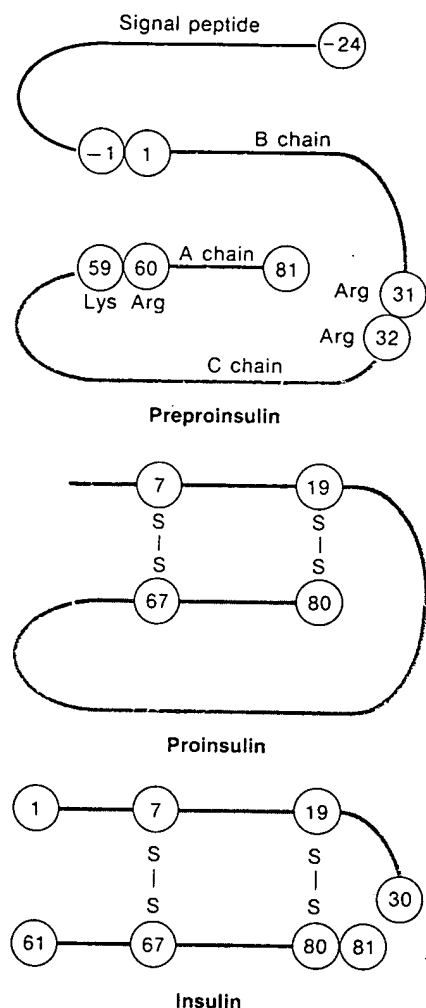
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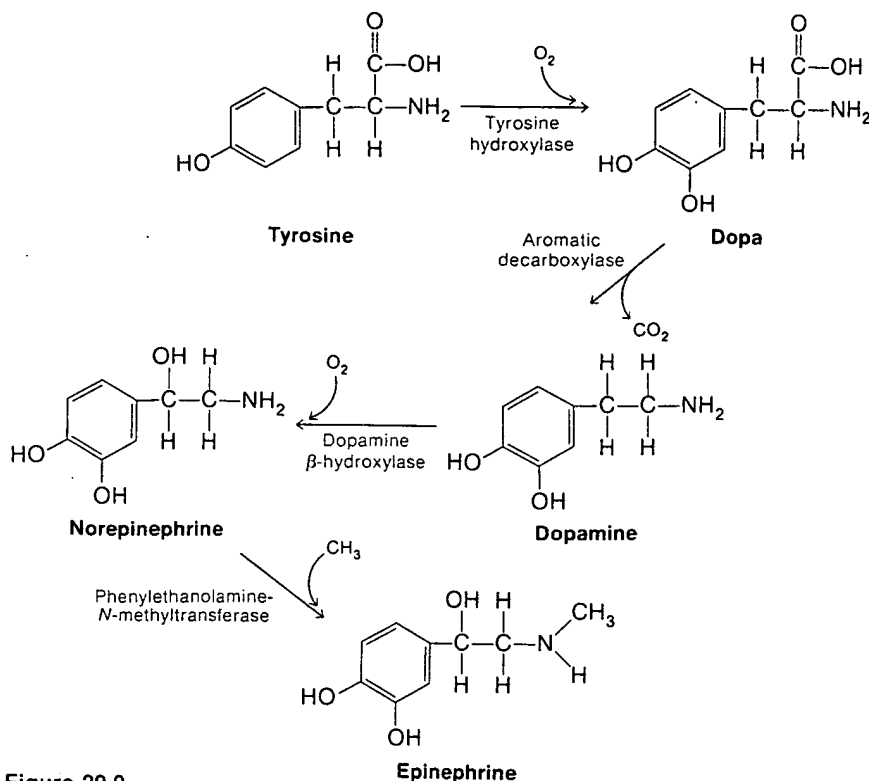
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**Figure 29-10**

Biosynthesis of insulin. Insulin is synthesized by membrane-bound polyosomes in the  $\beta$  cells of the pancreas. The primary translation product is preproinsulin, which contains a 24-residue signal peptide preceding the 81-residue proinsulin molecule. The signal peptide is removed by signal peptidase, cutting between Ala (-1) and Phe (+1), as the nascent chain is transported into the endoplasmic reticulum. Proinsulin folds and two disulfide bonds cross-link the ends of the molecule as shown. Before secretion, a trypsin-like enzyme cleaves after a pair of basic residues 31, 32 and 59, 60; then a carboxypeptidase B-like enzyme removes these basic residues to generate the mature form of insulin.



**Figure 29-9**

Pathway of catecholamine synthesis.

tyrosine to 3,4-dihydroxyphenylalanine (dopa), is catalyzed by tyrosine hydroxylase. This is the rate-limiting enzyme in the pathway, and its activity is controlled by a cAMP-dependent protein kinase. Epinephrine and norepinephrine are stored in chromaffin granules. These granules contain catecholamine and ATP in a molar ratio of 4:1 complexed with protein. Neural stimulation of the medulla is mediated by acetylcholine, which binds to receptors on the membranes of chromaffin cells and leads to a local depolarization and an influx of  $\text{Ca}^{2+}$ , and this results in the fusion of some chromaffin granules with the cell membrane and, consequently, extrusion of a packet of catecholamines and ATP into the circulation.

### Polypeptide Hormones Are Synthesized as Precursors

*All polypeptide hormones for which the mechanism of synthesis is known are synthesized as precursors.* The primary translation products of the mRNAs coding for insulin, glucagon, prolactin, growth hormone, gastrin, parathyroid hormone, vasopressin, and corticotropin have been characterized by cell-free translation, and in many cases, the mRNAs that code for these hormones have been cloned into bacterial plasmids and sequenced. In all these cases, *the primary translation product contains 20 to 30 predominantly hydrophobic amino acid residues at the amino terminus that*